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Synthesis and antibacterial activity of 6-benzyl-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-*7H*-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine

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Abstract

A new series of novel 6-benzyl-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***9(a-j)*** *in good to excellent yield by the reaction of 4-amino-5-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-4H-1,2,4-triazol- 3-ylhydrosulfide with a variety of phenacyl Iodides. The compounds of all the novel new compounds were established by IR,*^{1}*H,*^{13}*C-NMR,MS and elemental data. The compounds* ***9(a-j)*** *were evaluated for their antibacterial activity against four human pathogenic bacteria viz. Escherichia coli, Klebseilla pneumoniae, Shigella dysentriae and shigella flexnei. Amongst them, compounds containing (4-methylphenyl) moiety* ***9b,****(4-methoxyphenyl) moiety* ***9c,****(4-chlorophenyl) moiety* ***9d,****(4-dichlorophenyl) moiety* ***9f,****showed significant antibacterial activity, almost equal/more than the activity of the standard drug Streptomycin and Neomycin. All the compounds displayed significant activity against E.coli. Most of the novel new compounds showed appreciable activity against test bacteria as potential molecules for further development.*

Keywords: Synthesis,4-amino-5-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-4*H*-1,2,4-triazol- 3-ylhydrosulfide,6-benzyl-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4] triazolo[3,4-b][1,3,4]thiadiazine, Anti-bacterial activity.

INTRODUCTION

The establishment of 1,3,4-thiadiazine for drug discovery and industrial use has been shown to be very versatile. The uses for 1,3,4-thiadiazine have been found in different fields and are continuously improvement. The applications of these 1,3,4-thiadiazine are increasingly found in all aspects of drug discovery, ranging from cutting edge research through combinatorial chemistry and target-template *in situ* chemistry, to proteomics and DNA research using bio conjugation reactions. These 1,3,4-thiadiazine products are more than just passive linkers; they readily associate with biological targets, through hydrogen bonding and dipole interactions[1]. Derivatives of 1,3,4-thiadiazine have been found to have anti-HIV[2], anti-inflammatory[3] and anti-bacterial[4], anti-allergenic [5] activities. 1,3,4-thiadiazine are also being studied for the treatment of obesity[6] and osteoarthritis[7]. The increased interest in the 1,3,4-thiadiazine is due to it being non-toxic, benign and stable in biological systems[8].

1,3,4-thiadiazine are found in hydraulic fluids, and Photochemical products[9]. They have also been used as festicides[10],optical brightening agents, pigments and corrosion retardants[11-13]. This allows for the applications of 1,3,4-thiadiazine to grow exponentially due to their reliability, tolerance to a wide variety of functional groups, region specificity and the readily available starting materials. Through this, 1,3,4-thiadiazine are very attractive to use and apply in many fields.

A novel class of cationic anthraquinone analogs has been synthesized[14]. Among these compounds synthesized, some are exhibit broad antibacterial activity including MRSA and vancomycin resistant *Enterococcus faecalis* (VRE), which is comparable to other commercially available cationic antiseptic chemicals. A series of novel sulphanilamide derived 1,3,4-thiadiazine compounds has been synthesized and screened *in vitro* for their antibacterial and anti-

inflammatory activities[15]. Based on the wide spectrum of biological profile of 1,3,4-thiadiazine and triazolo their increasing importance in pharmaceutical, and biological field, and in continuation of our ongoing research on biologically active heterocyclic, it was thought of interest to accommodate triazolo and 1,3,4-thiadiazine moieties in a single molecular frame work to synthesize some new heterocyclic compounds with potential biological activity.

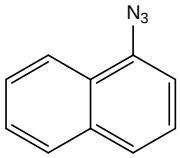
The present investigation deals with the synthesis A new series of novel 6-benzyl-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine **9(a-j)** in good to excellent yields by the reaction of 4-amino-5-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-4*H*-1,2,4-triazol- 3-ylhydrosulfide with a variety of phenacyl Iodides. The antibacterial activities of the compounds **9(a-j)** have also been evaluated.

MATERIALS AND METHODS

Reagents were of commercial grade and were used as supplied or were prepared according to procedures described in literature. Reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel F254 plates from Merck, and compounds visualized either by exposure to UV light. Chromatographic columns 60–120 mesh silica gel for separations were used. Melting points were determined on a Fisher–Johns apparatus and are uncorrected. IR spectra were recorded using KBr disk on a Perkin–Elmer FTIR spectrometer. The 1H NMR, ^{13}C NMR spectra were recorded on a Varian Gemini spectrometer (300 MHz for ^{1}H and 75 MHz for ^{13}C). Chemical shifts are reported in δ ppm units with respect to TMS as internal standard and coupling constants (*J*) are reported in Hz units. Mass spectra were recorded on a VG micro mass 7070H spectrometer. Elemental analyses (C, H, N) determined by means of a Perkin–Elmer 240 CHN elemental analyzer, were within ± 0.4% of theory.

Synthesis of Napthaleneazide (3)

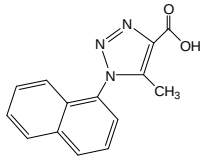
To a solution of Napthalene 1-amine **1** (10 mmol) in hydrochloric acid (25 mL), sodium nitrite solution was added drop wise at 0-5 ^{o}C and stirred for one hour to afford the diazonium chloride **2** and then cooled, stirred solution, a solution of sodium azide (25 mL) was added and stirring was continued for 30 min and the resulting solid was filtered and recrystallized from ethanol as yellow crystals.



IR (KBr): ν_{max} 3110, 2949, 2230, 1610 cm^{-1}.
^{1}H NMR ($CDCl_3$, 300 MHz): *δ* 7.10-7.20 (m, 4H, ArH),7.7(m,3H,ArH).
^{13}C NMR ($CDCl_3$, 75 MHz): *δ* 121.8,126.3,128.3,133.7,134.3, 135.0,141.2,144.2,146.2,150.2
MS: *m/z* 169 (M^+).
***Anal.* Calcd.** for $C_{10}H_8N_3$: C, 61.31; H, 4.213; N, 36.27. Found: C, 62.15; H, 4.12; N, 36.21.

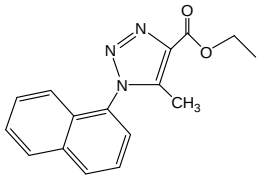
Synthesis of 5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazole-4-carboxylic acid (4)

A mixture of naphthalene azide **3** (0.1 mol) and ethyl acetoacetate (0.1 mol) in absolute ethanol (40 mL), and sodium ethoxide solution (20 mL) was refluxed for 4 h, the white solid which formed on heating was filtered and recrystallized from ethanol.



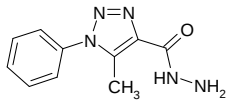
IR (KBr): ν_{max} 3450-3500, 3198, 2980, 2230, 1610 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): *δ* 2.35(s,3H,CH_3),7.10-7.20 (m, 4H, ArH),7.7(m,3H,ArH)
(m, 5H, ArH), 11.0 (s, 1H, COOH).
^{13}C NMR ($CDCl_3$, 75 MHz): *δ* 42.3,125.3,131.6,126.3,128.3,138.2,133.2,139.3,136.5,167.5.
MS: *m/z* 253 (M^+).
***Anal.* Calcd.** for $C_{14}H_{11}N_3O_2$: C, 60.12; H, 5.31; N, 20.18. Found: C, 60.02; H, 5.32; N, 21.72.

Synthesis of ethyl 5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazole-4-carboxylate (5)
To the solution of **4** (0.01 mole) in absolute thio ether (25 mL), conc. H_2SO_4 (2 mL) was added. The mixture was refluxed for 3 h. After completion of the reaction (TLC), the mixture was poured into ice-cold water. Crude product was collected by filtration, washed with 10% $NaHCO_3$ solution, dried and recrystallized from ethyl alcohol to get pure product **5** with 83% of yield, m.p. 158-60^{o}C.



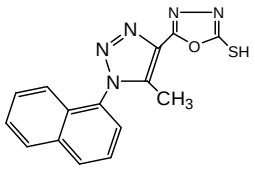
IR (KBr): ν_{max} 3010, 2943, 1698, 1621, 1513, 1249, 1034 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): δ1.24 (t, 3H, CH_3), 2.65 (s, 3H, CH_3), 4.17 (q, 2H, CH_2), 7.30-7.40 (m, 5H, ArH).
^{13}C NMR (DMSO-d_6 75 MHz): δ15.7, 59.7, 125.4, 128.0,128.9, 129.1, 134.5, 160.1.
MS: *m/z*280 (M^+).
***Anal*. Calcd.**for$C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.29; H, 5.61; N, 18.11.

Synthesis of 5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazole-4-carbohydrazide (6)
A mixture of compound **6** (0.01 mol) and hydrazine hydrate (0.025 mol) in ethanol (20 mL) was refluxed for 4 h, cooled to room temperature and filtered. The crude product was recrystallized from ethanol to give the new intermediate **7** in 70% of yield, m.p. 158-60^{o}C.



IR (KBr): ν_{max} 3010, 2943, 1698, 1621, 1513, 1249, 1034 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.30(t,3H, CH_3),2.35(s,3H,CH_3),4.67(q,2H,NH_2), 4.29(q,2H,CH_2),7.10-7.20 (m, 4H, ArH),7.7(m,3H,ArH), 8.0(s,1H,NH),
^{13}C NMR ($CDCl_3$, 75 MHz): δ14.1,42.3,60.9,125.3,126.3,131.6,132.3,134.7,137.2,140.3, 140.4,144.5.169.4.
MS: *m/z* 282 (M^+).
***Anal*. Calcd.** for $C_{16}H_{15}N_3O_2$: C, 61.32; H, 5.17; N, 18.26. Found: C, 63.21; H, 5.81; N, 18.34.

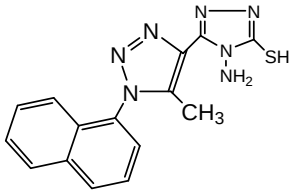
Synthesis of 5-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-1,3,4-oxadiazole-2-thiol (7)
A mixture of compound **6** (0.01 mol), potassium hydroxide (0.02 mol) and carbon disulfide (0.03 mol) in ethanol (100 mL) was heated under reflux with stirring for 12 h. The solvent was distilled *in vacuo*, the residual mass was poured over crushed ice and neutralized the alkaline solution with 10% hydrochloric acid. The precipitated crude product was filtered, washed with water, dried and recrystallized from ethanol to get the pure compound **7** in 78% yield, m.p. 146-148 ^{o}C.



IR (KBr): ν_{max} 3030, 2902, 2843, 1601, 1569, 1412, 1070 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.30(t,3H, CH_3), 2.35(s,3H,CH_3),3.0(s,1H,SH),4.29(q,2H,CH_2),7.10-7.20(m,4H,ArH), 7.7(m,3H,ArH),
8.0(s,1H,NH),
^{13}C NMR ($CDCl_3$, 75 MHz): δ14.1, 42.3, 60.9, 128.3, 132.6, 133.3, 135.3, 137.2, 139.5, 140.2, 143.3, 167.5, 168.4.
MS: *m/z* 309 (M^+).
***Anal*. Calcd.** for $C_{15}H_{11}N_5OS$: C, 51.91; H, 4.12; N, 28.32. Found: C, 51.86; H, 3.25; N, 26.68.

Synthesis of 4-amino-5-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-4H-1,2,4-triazole-3-thiol (8)
To a warm solution of compound **7** (0.01 mol) in ethanol (50 mL), 80% hydrazine hydrate (0.03 mol) was added drop wise and the reaction mixture was heated under reflux for 6 h. The solvent was distilled off *in vacuo*, cooled

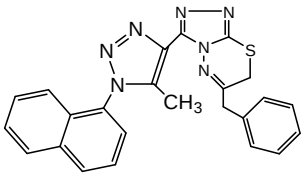
and the crystals separated were filtered, washed with cold ethanol and recrystallized from chloroform to give pure compound **8**, in 76% yield, m.p. 167-69 ^{o}C.



IR (KBr): ν_{max} 3343, 3068, 1663, 1460, 1030 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.30(t,3H, CH_3), 2.0(s,2H,NH_2),2.35(s,3H,CH_3), 3.0(s,1H,SH),4.29(q,2H,CH_2),7.10-7.20(m,4H,ArH),7.7(m,3H,ArH),8.0(s,1H,NH).
^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.1, 42.3, 59.9, 60.5, 133.3, 134.6, 135.3, 138.3, 140.2, 142.2, 147.3, 150.5, 154.6,167.5, 169.4.
MS: *m/z* 323 (M^+).
***Anal*. Calcd.** for $C_{15}H_{13}N_7S$: C, 51.42; H, 4.17; N, 36.17. Found: C, 51.19; H, 3.98; N, 34.99.

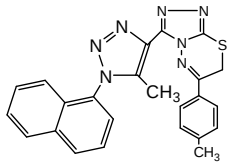
General procedure for the synthesis of 6-benzyl-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine 9(a-j):
A mixture of compound **8** (0.01 mol) and corresponding phenacyl iodides (0.02 mol) in absolute ethanol (20 mL), was refluxed for 6 h. The reaction mixture was concentrated and cooled to room temperature, and the remaining solvent was removed under reduced pressure, then diethyl ether (25 mL) was added and the reaction mixture was left at 5^{0}C for overnight. The precipitated solid was filtered off; the crude product thus obtained was purified by column chromatography on silica gel with hexane-ethyl acetate as eluent to afford pure compounds **9(a-j)** in 74-84% of yields.

Synthesis of 6-benzyl-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine (159a):



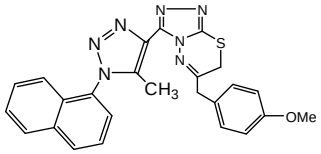
IR (KBr): ν_{max} 3031, 1624, 1590, 1457 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.30(t,3H, CH_3), 2.0(s,2H,NH_2),2.35(s,3H,CH_3), 3.0(s,1H,SH),3.1(s,2H,CH_2),2.3(s,2H,CH_2),4.21(s,2H,CH_2-S),4.29(q,2H,CH_2),7.10-7.20(m,4H,ArH),7.7(m,3H,ArH),8.0(s,1H,NH),
^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.1, 36.0,45.3, 51.9, 59.5,121.3, 128.6, 131.3, 135.3, 138.2, 140.2, 142.3, 145.5, 149.6,161.5, 168.4.
MS: *m/z* 425 (M^+).
***Anal*. Calcd.** for $C_{24}H_{19}N_7S$: C, 63.45; H, 5.16; N, 27.56. Found: C, 62.71; H, 5.01; N, 25.26.

Synthesis of 3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-6-p-tolyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine (9b):



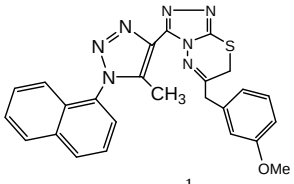
IR (KBr): ν_{max} 3032, 1610, 1591, 1530, 1032, 746 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.30(t,3H, CH_3), 2.0(s,2H,NH_2),2.35(s,3H,CH_3), 3.0(s,1H,SH),3.1(s,2H,CH_2),2.3(s,2H,CH_2),4.21(s,2H,CH_2-S),4.29(q,2H,CH_2),7.10-7.20(m,4H,ArH),7.7(m,3H,ArH),8.0(s,1H,NH).
^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.1, 39.0,45.3, 57.9, 59.5,121.3, 129.6, 133.3, 138.3, 142.2, 148.2, 152.3, 155.5, 161.6,163.5, 169.4.
MS: *m/z* 439 (M^+).
***Anal*. Calcd.** for $C_{24}H_{19}N_7S$: C, 61.99; H, 5.19; N, 26.29. Found: C, 62.16; H, 4.17; N, 26.17.

Synthesis of 6-(4-methoxybenzyl)-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo [3,4-b][1,3,4]thiadiazine (9c):



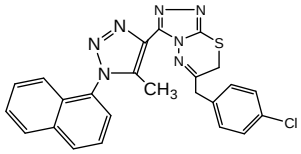
IR (KBr): ν_{max} 3035, 1620, 1596, 1535, 1070, 1030, 747 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.30(t,3H, CH_3), 2.0(s,2H,NH_2),2.35(s,3H,CH_3), 3.0(s,1H,SH),3.1(s,2H,CH_2),2.3(s,2H,CH_2),3.20(s.3H,O-CH_3),4.21(s,2H,CH_2-S), 4.29(q,2H,CH_2),7.10-7.20(m,4H,ArH),7.7(m,3H,ArH),8.0(s,1H,NH),
^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.1, 35.0,43.3, 52.9, 62.5,121.3, 129.6, 130.3, 131.3, 136.2, 138.2, 141.3, 146.5, 147.6,149.5, 161.4,169.1.
MS: *m/z* 467 (M^+).
***Anal*. Calcd.** for $C_{25}H_{21}N_7OS$: C, 61.31; H, 5.31; N, 23.15. Found: C, 60.50; H, 4.32; N, 21.25.

Synthesis of 6-(3-methoxybenzyl)-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo [3,4-b][1,3,4]thiadiazine (9d):



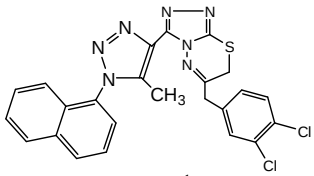
IR (KBr): ν_{max} 3034, 1617, 1592, 1541, 1070, 1032, 745 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.30(t,3H, CH_3), 2.0(s,2H,NH_2),2.35(s,3H,CH_3), 3.0(s,1H,SH),3.1(s,2H,CH_2),2.3(s,2H,CH_2),3.20(s.3H,O-CH_3),4.21(s,2H,CH_2-S),4.29(q,2H,CH_2), 7.10-7.20(m,4H,ArH),7.7(m,3H,ArH),8.0(s,1H,NH).
^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.1, 36.0,42.3, 60.9, 67.5,125.3, 131.6, 126.3, 128.3, 138.2, 133.2, 139.3, 136.5, 145.6,167.5, 135.4.
MS: *m/z* 467 (M^+).
***Anal*. Calcd.** for $C_{25}H_{21}N_7OS$: C, 60.01; H, 4.35; N, 23.99. Found: C, 60.50; H, 4.31; N, 25.32.

Synthesis of 6-(4-chlorobenzyl)-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine (9e):



^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.30(t,3H, CH_3), 2.0(s,2H,NH_2),2.35(s,3H,CH_3), 3.0(s,1H,SH),3.1(s,2H,CH_2),2.3(s,2H,CH_2),4.21(s,2H,CH_2-S),4.29(q,2H,CH_2),7.10-7.20(m,4H,ArH),7.7(m,3H,ArH),8.0(s,1H,NH).
^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.9, 33.0,45.3, 59.9, 61.5,122.3, 133.6, 135.3, 137.3, 138.2, 142.2, 145.3, 149.5, 151.6,158.5, 161.4.
MS: *m/z* 469 (M^+).
***Anal*. Calcd.** for $C_{24}H_{18}N_7SCl$; C, 56.91; H, 3.17; N, 25.12. Found: C, 56.91; H, 3.30; N, 25.19.

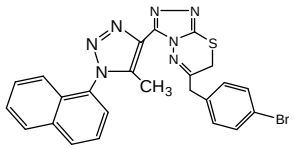
Synthesis of 6-(3,4-dichlorobenzyl)-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo [3,4-b][1,3,4]thiadiazine (9f):



IR (KBr): ν_{max} 3035, 1618, 1590, 1532, 1030, 750, 680 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.30(t,3H, CH_3), 2.0(s,2H,NH_2),2.35(s,3H,CH_3), 3.0(s,1H,SH),3.1(s,2H,CH_2),2.3(s,2H,CH_2),4.29(q,2H,CH_2),7.10-7.20(m,4H,ArH),7.7(m,3H,ArH),8.0(s,1H,NH), 11.0 (s, 1H, COOH).

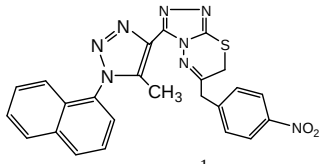
^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.1, 36.0,42.3, 60.9, 67.5,125.3, 131.6, 126.3, 128.3, 138.2, 133.2, 139.3, 136.5, 145.6,167.5, 135.4.
MS: *m/z* 501 (M^+).
***Anal*. Calcd.** for $C_{24}H_{17}Cl_2N_7S$: C, 56.51; H, 4.06; N, 27.16 Found: C, 52.13; H, 4.90; N, 23.12.

Synthesis of 6-(4-bromobenzyl)-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine (9g):



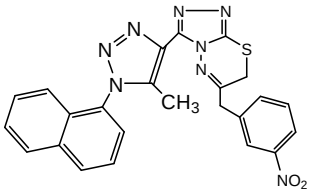
IR (KBr): ν_{max} 3030, 1611, 1586, 1530, 1030, 586 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.30(t,3H, CH_3), 2.35(s,3H,CH_3), 3.1(s,2H,CH_2),2.3(s,2H,CH_2),4.25(s,2H,CH_2-S),4.49(q,2H,CH_2),7.10-7.20(m,4H,ArH),
7.7(m,3H,ArH).
^{13}C NMR ($CDCl_3$, 75 MHz): δ 12.2, 24.0,39.3, 61.9, 62.5,120.3, 121.6, 125.3, 126.3, 127.2, 128.2, 129.3, 132.5, 142.6,144.5, 149.4.
MS: *m/z* 515 (M^+).
***Anal*. Calcd.** for $C_{24}H_{18}N_7SBr$: C, 50.45; H, 3.12; N, 21.68. Found: C, 50.40; H, 3.06; N, 21.60.

Synthesis of 6-(4-nitrobenzyl)-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine (9h):



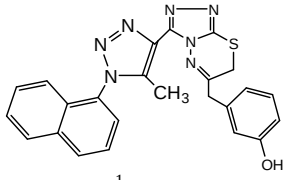
IR (KBr): ν_{max} 3035, 1618, 1595, 1532, 1370, 1030, 749 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.30(t,3H, CH_3), 3.0(s,1H,SH),3.1(s,2H,CH_2),2.3(s,2H,CH_2),4.0(s,2H,CH_2-S),4.29(q,2H,CH_2),7.10-7.20(m,4H,ArH),7.7(m,3H,ArH).
^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.1, 36.0,45.3, 60.9, 67.5,125.3, 131.6, 126.3, 128.3, 133.2, 135.4. 136.5, 138.2, 139.3, 145.6,167.5.
MS: *m/z* 482 (M^+).
***Anal*. Calcd.** for $C_{24}H_{18}N_8O_2S$: C, 59.51; H, 4.51; N, 28.18. Found: C, 59.49; H, 4.31; N, 27.70.

Synthesis of 6-(3-nitrobenzyl)-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine (9i):

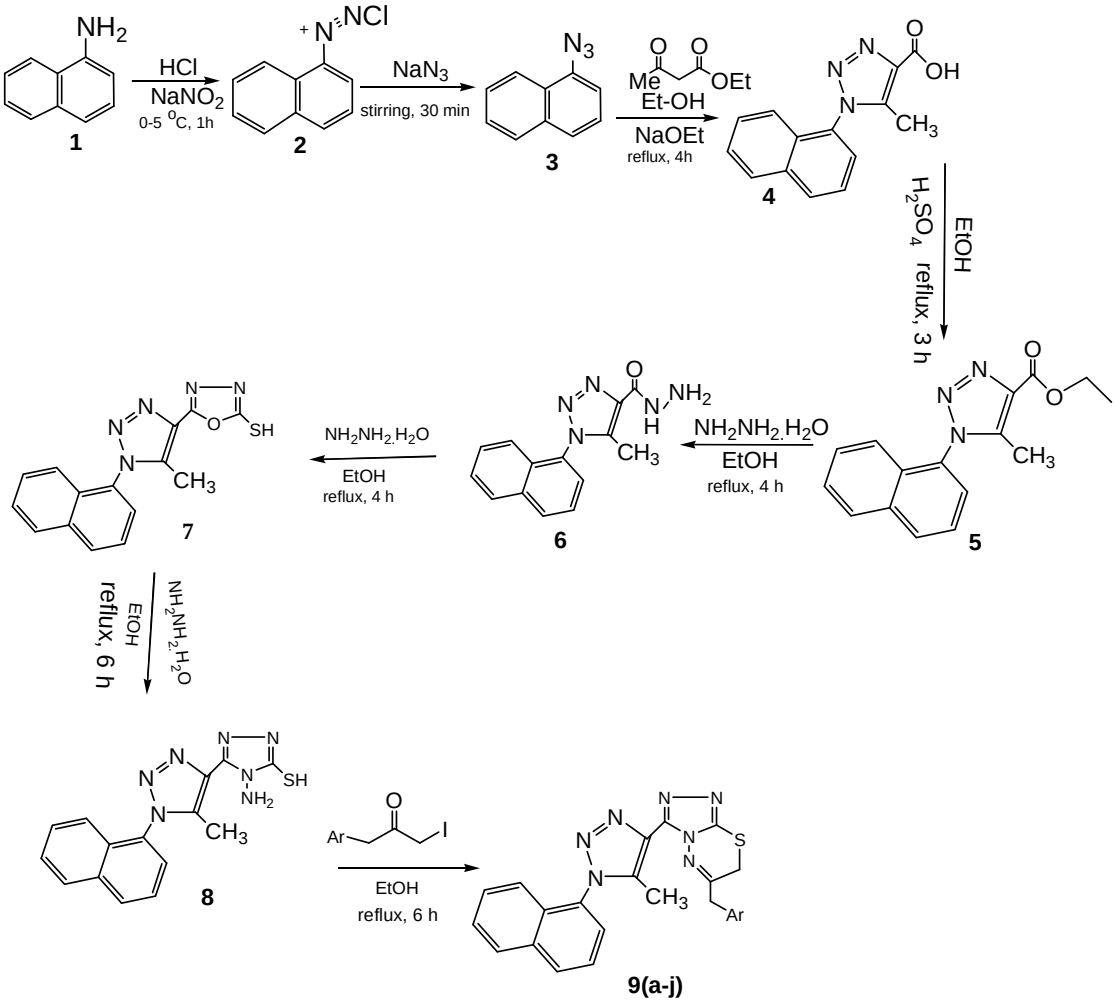


IR (KBr): ν_{max} 3035, 1614, 1590, 1520, 1370, 1030, 746 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.30(t,3H, CH_3), 2.0(s,2H,NH_2),2.35(s,3H,CH_3),
3.0(s,1H,SH),3.1(s,2H,CH_2),2.3(s,2H,CH_2),4.29(q,2H,CH_2),7.10-7.20(m,4H,ArH),7.7(m,3H,ArH),8.0(s,1H,NH),
11.0 (s, 1H, COOH).
^{13}C NMR ($CDCl_3$, 75 MHz): δ 15.1, 26.0,32.3, 50.9, 57.5,121.3, 122.6, 123.3, 126.3, 128.2, 129.2, 131.3, 132.5, 139.6,140.5, 167.4.
MS: *m/z* 482 (M^+).
***Anal*. Calcd.** for $C_{24}H_{18}N_8O_2S$: C, 59.59; H, 4.69; N, 28.79. Found: C, 59.49; H, 4.31; N, 27.70.

Synthesis of 3-((3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo[3,4-b][1,3,4] thiadiazin-6-yl)methyl)phenol (9j):



IR (KBr): ν_{max} 3310, 3035, 1618, 1596, 1030, 746 cm^{-1}.
^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.30(t,3H, CH_3), 3.1(s,2H,CH_2-S),2.3(s,2H,CH_2),4.29(q,2H,CH_2),7.10-7.20(m,4H,ArH),7.7(m,3H,ArH),8.0(s,1H,OH).
^{13}C NMR ($CDCl_3$, 75 MHz): δ 15.1, 37.0,38.3, 50.9, 57.5,120.3, 121.6, 122.3, 123.3, 124.2, 125.2, 126.3, 127.5, 128.6,135.5, 165.4.
MS: *m/z* 453 (M^+).
***Anal*. Calcd.** for $C_{24}H_{19}N_7OS$: C, 59.62; H, 4.98; N, 26.72. Found: C, 59.14; H, 4.73; N, 26.12.



*9: Ar= **(a)**4-I-C_6H_4; **(b)** 4-C_2H_5-C_6H_4; **(c)** 4-C_2H_5O-C_6H_4; **(d)** 3-C_2H_5O-C_6H_4; **(e)** 3-Cl-C_6H_4; **(f)** 4-(Cl)-C_6H_4; **(g)**3-Br-Furyl; **(h)** 4-NO_2-Furyl; **(i)** 3-NO_2-Furyl; **(j)** 4-OH-Furyl;*

RESULTS AND DISCUSSION

The diazotization of Napthalene 1-amine **1** by nitrous acid at 0-5 ^{0}C lead to the formation of naphthalene diazonium chloride **2**, which on reaction with sodium azide produced naphthalene azides **3** in 82% yield. It was reported that the azide compound can be cyclized using ethyl acetoacetate to furnish 1,2,3-triazole derivative. In a similar fashion naphthalene azide compound **3** was cyclized with ethyl acetoacetate in the presence of sodium ethoxide to afford another intermediate, 5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazole-4-carboxylic acid **4** in 78% yield. 5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazole-4-carboxylic acid **4** was reacted with absolute thio Ether in the presence of catalytic amount of conc. H_2SO_4 at reflux for 3 h, to get the ethyl 5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazole-4-

carboxylate **5** in 83% yield. The intermediate, 5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazole-4-carbohydrazide **6** was prepared on hydrazinolysis of compound **5** with hydrazine hydrate, in ethyl alcohol at reflux for 4 h, with 77% of yield. 5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazole-4-carbohydrazide **6** was reacted with carbon disulfide in the presence of potassium hydroxide, in ethanol at reflux for 12 h, followed by acidification gave the 5-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-1,3,4-oxadiazole-2-thiol **7** in 78% of yield. Compound **7** when reacted with hydrazine hydrate, in ethanol at reflux for 6 h, resulted the 4-amino-5-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-4H-1,2,4-triazole-3-thiol **8** in 76% of yield. Further, the 4-amino-5-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-4H-1,2,4-triazole-3-thiol **8** has been condensed successively with a variety of phenacyl iodides in ethyl alcohol under reflux for 6 h to get the title compounds, 6-benzyl-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine **9 (a-j).**

Antibacterial Activity

The 6-benzyl-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine **9(a-j)** were screened for their antibacterial activity against four human pathogenic bacteria *viz*., *Escherichia coli*, *Klebseilla pneumoniae*, *Shigella dysentriae* and *Shigella flexnei*. The zone of inhibition in mm at concentration 100 μg/mL was determined using the cup-plate method Standard antibacterial agents such as streptomycin and neomycin, were also screened under similar conditions for comparison and the results are presented in **Table 1**.

Table 1: Antibacterial activity of 9(a-j)

Compound	zone of inhibition in mm at 100 μg/mL			
	E. coli	*K. pneumoniae*	*S. dysentriae*	*S. flexnei*
9[a]	24	22	21	22
9b	23	22	21	26
9c	32	27	28	27
9d	24	20	25	20
9e	20	21	22	22
9f	21	22	23	24
9g	15	18	19	12
9h	18	16	14	13
9i	16	17	16	13
9j	19	13	18	16
Streptomycin	30	30	30	30
Neomycin	20	20	20	20
Note: <16 mm, inactive; 17-20 mm, moderately active; 20-27mm, highly active.				

The antibacterial screening data of the compounds **9(a-j)** showed that the compounds **9b**, **9c**, **9d**, **9e** and **9f** were highly active against all the organism employed. Compound **9c** is highly active against all the test organisms employed and the zone of inhibition is more than the standard drug Neomycin, and almost equal to the standard drug streptomycin. The other compounds showed moderate to good activity against these organisms employed. All the compounds displayed significant activity against *E. coli*.

CONCLUSION

In conclusion, we have described the synthesis of novel 6-benzyl-3-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine **9(a-j)** in good to excellent yields 74-84% by the reaction of 4-amino-5-(5-methyl-1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)-4H-1,2,4-triazole-3-thiol **8** and corresponding phenacyl Iodides. Some of these compounds exhibit excellent antibacterial activities and can be evaluated as antibacterial agents.

Acknowledgements
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